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ACTION OF ADRENALIN ON THE SPLEEN

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It is generally agreed by recent investigators (1) that adrenalin causes dilatation of the blood vessels in certain parts of the organism. It has been found from experiments carried out in this laboratory that this dilatation is caused, at least in part, by the action upon sympathetic and dorsal root ganglia (2). It may also be caused as shown by Gruber (3) and confirmed by us (4) that the dilatation may result from the stimulation of some peripheral tissue, perhaps myoneural junctions of dilator fibres. It is not possible to say which is more important in producing dilatation normally, the "gangliar" mechanism or the myoneural junction. In some animals the same amount of dilatation has been obtained by the action of adrenalin upon the gangliar portion of the mechanism alone (limb perfused, adrenalin injected into the jugular vein) as occurred from the injection of the same quantity when the circulation was intact (4).

Cats and dogs have been used principally for adrenalin experiments, but work recently published from this laboratory (5) has shown this reaction to be common to Marsupials, Ungulates, and Primates, Rodents being an exception. Therefore physiologists can no longer dismiss adrenalin vasodilatation as an interesting exception.

A careful study has been made of the "gangliar-terminal" action in the hind limb (4), but in many other organs this has not been done. It is the purpose of this and succeeding researches to make a further study of this question in various organs. The present paper is confined to the spleen.

METHODS

Volume changes in the spleen were recorded by enclosing the organ in a gutta percha oncometer connected to a bellows of the Brodie type. The flexible part of the latter was made of rubber cut from a condom. This was fastened to the edge of the bellows base and top with thin glue except at the back where the hinge is located, and where the overlap occurs rubber cement must be used, because the glue when dry stiffens the rubber. Formerly rubber cement was used throughout, but the curling which it causes renders the bellows very difficult to make. The lever for the writing point was attached at right angles to the top of the bellows.

The nerves and blood vessels were carefully freed from fat and connective tissue and then grouped so as to form a double stalk. In many cases it was possible to do this without tying any blood vessels. The spleen was placed in a double-necked oncometer (1e) which was covered with a glass plate connected to the transmission tube.

For perfusion we used one of the large arteries which supplied about one-half of the spleen, the remaining arteries being tied off. Warmed oxygenated Ringer's solution was perfused under a constant pressure produced by compressed air. The temperature and pressure of the perfusion fluid were registered at the entrance to the cannula.

Ether was used as the anaesthetic. Adrenalin solutions were made by diluting Parke, Davis and Company's adrenalin chloride solution with distilled water.

RESULTS

In an earlier research (1e) we made a careful study of the normal spleen in its reaction to adrenalin injected intravenously; seven dogs gave nothing but constriction, while three others responded by dilatation or dilatation and constriction. There seemed to be some question as to the occurrence of active dilatation in the spleen, because in two of the animals, the dilatation preceded the constriction and therefore might be a passive

FIG. 1. WAVES PRODUCED IN A PRACTICALLY QUIESCENT SPLEEN BY THE INJECTION OF A DIMINISHED DOSE OF ADRENALIN, 0.2 CC., 1: 100,000. CAT 2.5 KGM.

effect due to constriction elsewhere. Dilatation followed constriction in only one spleen and that was after a large dose of adrenalin.

We have studied four more normal spleens, two of the dog, two of the cat; all but one cat gave dilatation with some dose of adrenalin. In this animal (2.5 kgm.) no dilatation could be secured from a range of doses starting with 0.1 cc., 1:100,000 adrenalin and running as high as 0.5 cc., 1:10,000, however after many of the injections the amplitude of the splenic waves

FIG. 2. WAVES PRODUCED IN A QUIESCENT SPLEEN BY THE INJECTION OF A PRESSOR DOSE OF ADRENALIN, 0.5 CC., 1:10,000. CAT 2.5 KGM.

was increased, although the initial effect might be a partial inhibition of the waves. Again the splenic waves might be practically absent until adrenalin was injected, after which they became very marked (fig. 1). Even pressor doses produced a similar effect (fig. 2).

In a second cat (3.7 kgm.) slight dilatation always preceded the constriction which in many cases was followed by waves. Small doses such as 0.1 cc., to 0.5 cc., 1:10,000,000 caused dilatation only.

Although dilatation usually preceded constriction in the two dogs, it occasionally followed the constriction in one animal.

It seemed possible that dilatation of the spleen as in the intestine might be caused by stimulation of the ganglia supplying it. In order to find out whether structures not located in the spleen, could be the cause of the dilatation, we tied all of the blood vessels, and then perfused a portion of it through one of the largest arteries, the outflow being from a vein which had been cut open. Great care was taken to preserve the nerve supply. In this way the effects of adrenalin could be observe either solely upon structures in the spleen by injection into the perfusion fluid or upon structures located outside of the spleen by injection into the general circulation.

We perfused three spleens. The first belonged to a dog weighing 22 kgm. and gave the following responses:

DOSE	PLACE OF INJECTION	RESPONSE IN BLOOD PRESSURE IN MM. OF MERCURY	RESPONSE OF THE SPLEEN
1.0 cc. 1: 100,000	Jugular vein	180–180–156	Dilatation
3.0 cc. 1: 100,000	Jugular vein	177–190–154	Dilatation
5.0 cc. 1: 100,000	Jugular vein	188–194–164	Marked dilatation
1.0 cc. 1: 10,000	Jugular vein	188–210–166	Marked dilatation
0.2 cc. 1: 1,000,000	Through perfusion fluid	None	Constriction, very marked
0.1 cc. 1: 1,000,000	Through perfusion fluid	None	Constriction, marked
0.1 cc. 1: 10,000,000	Through perfusion fluid	None	No effect

The perfused spleen of this animal dilated with every dose of adrenalin injected into the jugular vein (fig. 3), but constricted with each injection into the perfusion fluid (fig. 4). The latter was injected into the fluid just before it entered the cannula. The pressure for perfusion was 45 mm. of mercury while the temperature was 33.4°C.

The second spleen did not seem to be responding very well and no effect could be obtained except a slight constriction when adrenalin was introduced into the general circulation.

The third perfused spleen, belonging to a dog weighing 10 kgm., dilated considerably with the doses of adrenalin injected

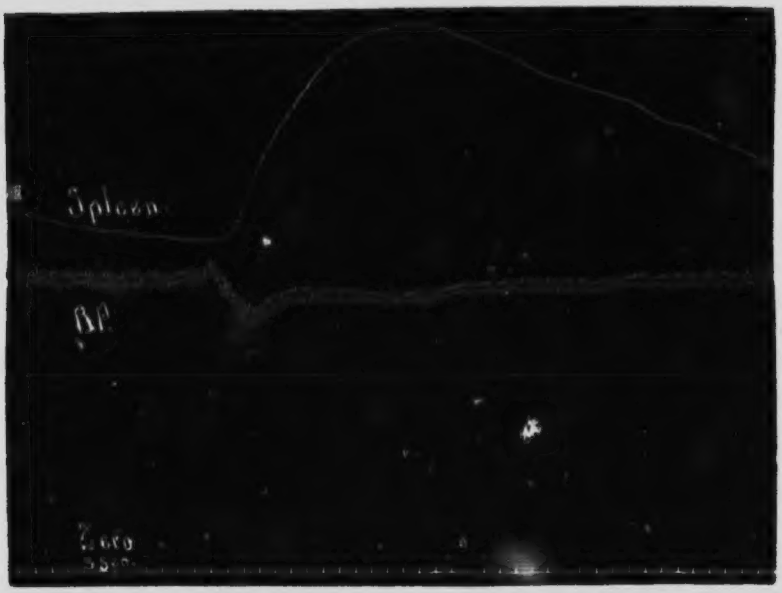

FIG. 3. DILATATION OF A PERFUSED SPLEEN FROM THE INJECTION OF 5.0 CC. 1:100,000 ADRENALIN INTO THE JUGULAR VEIN. DOG 22 KGM.

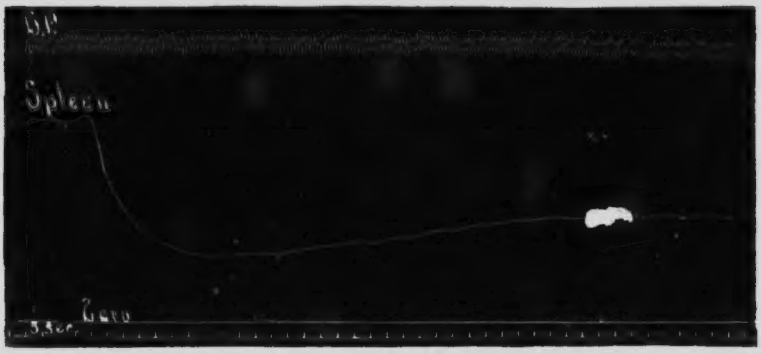

FIG. 4. CONSTRICTION OF A PERFUSED SPLEEN FROM THE INJECTION OF 0.1 CC., 1:1,000,000 ADRENALIN INTO THE PERFUSION FLUID. DOG 22 KGM.

into the jugular vein, 0.5 cc., 1:100,000 to 0.5 cc., 1:10,000. These doses were depressor in their effect upon the blood pressure. When adrenalin was injected into the perfusion fluid, constriction was followed by dilatation (fig. 5). This was true even with a relatively large dose, 0.2 cc. 1:100,000. The dilatation, however, was not as marked as that produced from the mechanisms outside of the spleen.

FIG. 5. CONSTRICTION FOLLOWED BY DILATATION, PRODUCED BY THE INJECTION OF ADRENALIN INTO THE PERFUSION FLUID ENTERING A PERFUSED SPLEEN.

First injection 0.2 cc., 1:1,000,000; second injection, 0.2 cc., 1:100,000. Dog 10 kgm.

In order to determine whether the semilunar ganglion contained mechanisms which might cause dilatation of the spleen through the action of adrenalin, direct application of adrenalin to this ganglion was tried while the spleen was in an oncometer with its circulation intact. If no changes in blood pressure occurred during the experiment we were justified in assuming that adrenalin was not passing into the blood stream and there-

fore could produce its effect only by gangliar action. Absorption was facilitated by slitting the surface of the ganglion.

The spleen of a cat was studied by this method. Solutions of 1:100,000 were twice applied without changing the blood pressure, but in each instance causing dilatation of the spleen. A third application of a stronger solution caused a very marked dilatation (fig. 6).

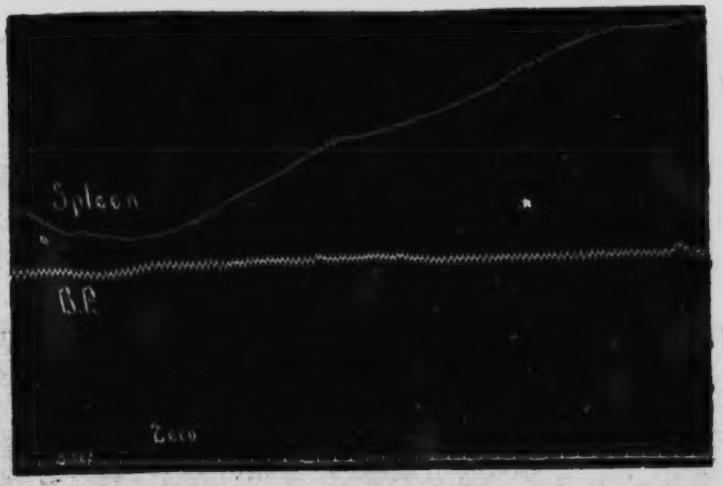

FIG. 6. DILATATION OF THE SPLEEN CAUSED BY THE DIRECT APPLICATION OF 1:10,000 ADRENALIN TO THE SEMILUNAR GANGLION. CAT.

This experiment therefore demonstrates that the semilunar ganglion is one location of the adrenalin dilator mechanism of the spleen.

We also studied the effect of adrenalin upon the spleen through action upon the ganglia of the dorsal nerve roots. These ganglia were exposed and painted with solutions of adrenalin after cutting the connections with the spinal cord. In some instances the ganglia were split open to facilitate absorption. Blood pressure records were taken at the same time. Care must be taken not to stimulate the ganglia mechanically, for sometimes that will cause splenic volume changes. The twelfth and thirteenth thoracic ganglia on the left side were almost always used.

Five cats were studied. All showed some response to adrenalin applied to the above ganglia, although in some instances only one response could be obtained from a single ganglion, a new ganglion being required in that case to secure a repetition of the response. The volume changes are usually slow in occurring and likewise slow in disappearing unless the ganglion is washed to remove the adrenalin.

One animal responded by dilatation only with concentrations of 1: 10,000 and 1: 1000; weaker solutions were not tried.

Three of them gave dilatation sometimes and constriction at other times, there being no regularity in the occurrence of either.

The fifth cat was interesting in that adrenalin applied to the ganglia in question, caused waves in the spleen if it were quiescent, or increased the amplitude of the waves if they were already present.

We would conclude from our observations that both constrictor and dilator mechanisms for the spleen are present in the dorsal root ganglia. We cannot say which predominates.

DISCUSSION

Oliver and Schäfer (6) were the first to study the action of adrenalin (adrenal extract) upon the spleen. In no cases did they obtain a dilatation except "a very slight preliminary expansion," probably caused by the increased heart's action. A later paper by Schäfer and Moore (7) added to this observation that the after effect of the injection was to increase the extent of the normal rhythmic movements. When injected into a perfused spleen a strong contraction was obtained.

Bardier and Fränkel (8) obtained dilatation from macerated adrenals. Others (9) speak only of contraction of the spleen from adrenalin.

Recently Hoskins and Gunning (1c) and Hartman and McPhedran (1e) have observed mainly constriction from adrenalin in the spleen. The former speak of a brief dilatation followed by contraction. They occasionally obtained an active dilatation following the constriction.

Our experiments have proven that dilatation from adrenalin can be obtained by action upon structures in the semilunar ganglion, and the dorsal root ganglia as well as by action upon structures in the spleen. In this respect the adrenalin dilator mechanism of the spleen is similar to that of skeletal muscle (as shown by the hind limb, 4).

There can now be no doubt that adrenalin produces active dilatation of the spleen. Judging from our experiments the gangliar mechanism gives the dilator effects more easily than does the peripheral mechanism. That may be due to a partial masking of the dilator mechanism by the constrictor mechanism in the latter region.

In regard to the peripheral effect there seems to be a distinct difference between the limb reaction and that of the spleen. In the perfused limb small amounts of adrenalin injected into the perfusion fluid cause pure dilatation, larger amounts may cause dilatation followed by constriction, while very large doses may cause pure constriction. On the other hand in the perfused spleen if dilatation is obtainable from adrenalin injected into the perfusion fluid, it follows constriction, at least in our experience.

SUMMARY

1. Dilatation of the spleen is caused by the action of adrenalin upon the twelfth and thirteenth dorsal root ganglia, the semilunar ganglion or upon some terminal structure in the spleen itself.

2. Constriction from adrenalin can result from the response of a mechanism in the dorsal root ganglia or from a structure in the spleen.

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